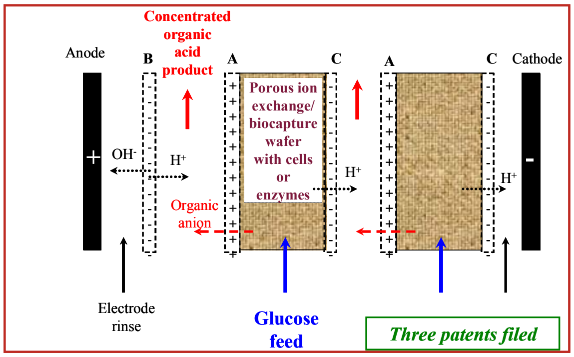
A Membrane-Based Separative Bioreactor

Integrating bioconversion and downstream processing

Biotechnology is transforming the chemical industry and Argonne is at the forefront with the membrane-based separative bioreactor. The separative bioreactor enables direct capture of high-purity products from pH controlled fermentations *without* the need for neutralization. Organic chemicals are used in the U.S. for everything from plastics to solvents. By in large, these chemicals are derived from petroleum. The Dept. of Energy supports research to decrease dependence on imported petroleum by looking to biomass and other renewable resources as an alternative feedstock. Biological feedstocks are more suited for conversion and processing by biological means. Thus the chemical industry is embracing biotechnology and bioprocessing.

Bioprocessing offers several distinct advantages over chemical processing including more benign solvents and temperature conditions, lower energy usage, greater choice in feedstocks and products. Bioprocessing has some significant technical/ economic barriers to overcome for widespread acceptance. The largest barriers are associated with the complexity of downstream processing (separations and purification). This complexity arises from the byproducts generated by metabolism as well as media nutrients that must be separated from the desired products. Other restricting factors are product inhibition of the biocatalyst, and stability of the biocatalyst.

Separative Bioreactor

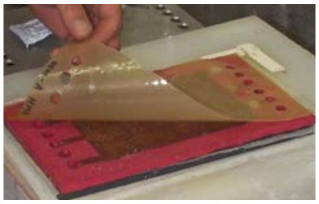


- pH controlled reactions
- Direct capture and concentration of charged products
- Avoid product inhibition
- Removal of charged impurities
- Sequential reactions
- Reduced waste streams
- ***Fermentations without buffering***

Metabolic organic acids such as acetic or lactic acid are extremely large volume products that could be produced by bioprocessing. In conventional bioprocessing, these acids must be neutralized with sodium or calcium to avoid biocatalyst shut down. Neutralization creates salt products rather than the desired acids. Conversion back to the acid generates significant waste. Using biological cells as the model, Argonne redesigned the fundamental approach to fermentation. Cells produce acids as a part of normal metabolism and use proton motive force to export the acids across cell membranes. Argonne uses electrical force to transport organic acids away from the biocatalyst across an ion exchange membrane and into a concentrate chamber.

Work with direct enzyme immobilization on membranes revealed excellent product separations, but insufficient enzyme density limited overall performance. To increase enzyme density, we turned to our electrodeionization (EDI) technology for electrically-driven desalination. We molded loose ion exchange resin beads into a patented porous resin wafer. This resin wafer enables capture of charged species (salts, acids) at dilute levels with high energy efficiency and reduced waste streams in comparison to conventional processing (Field demonstrated, Patent 6,495,014 and 2002 R&D 100 Award).

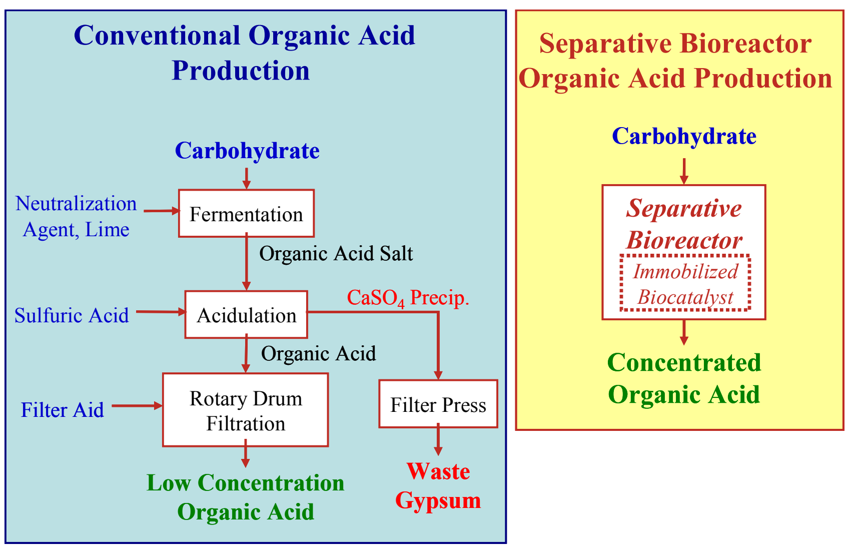
Patented resin wafer



In designing the separative bioreactor, we incorporated enzyme capture resin beads into the resin wafer. Sugars were converted by the immobilized biocatalyst to the target acids, and the product was electrically transported into a concentrate channel. *Remarkably, the reactions could be run without buffering or neutralization.* Acid capture enabled us to control reactor pH at the optimum level enhancing biocatalytic performance. In fact, the target pH could be computer modeled and then achieved in the laboratory. Additionally, enzymatic activity was increased in the wafer because product capture and removal avoided biocatalyst inhibition. Reactions were run continuously for days, ceasing only when the captured product reached saturation. Argonne's immobilization technology allows *in situ* stripping and replacement of degraded enzyme without disassembling the system. Enzyme recharging extends operation time between service cycles.

Argonne's initial analysis indicates that the separative bioreactor will dramatically reduce the cost of producing chemicals by bioconversion. Biobased products that are not currently economically feasible could prove practical with our technology.

Separative Bioreactor Flowchart
Simplified Processing = Superior Performance



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